Department of Environmental & Toxicologic Pathology

Nelson S. Irey, M.D.
Chairperson
Date of Appointment - 10 February 1966

MISSION

To conduct a program of consultation, education, and research in the areas of environmental, drug-induced, and radiation pathology, as well as development and application of toxicological (biochemical) techniques for analysis of tissue and determination of the causes of injury to human and animal tissue.

This department is divided into five divisions:

1. Biochemistry Division - Dr. William Fishbein.
2. Chemical Division - Dr. Frank Johnson
3. Environmental Toxicologic Division - Dr. Victor Kalasinsky
4. Environmental Pathology Division - Dr. Nelson S. Irey and Dr. Florabel G. Mullick
5. Mutagenic Division - Dr. David Busch

STAFF

Nelson S. Irey, M.D., Chairperson
Florabel G. Mullick, M.D., Staff Pathologist
(A) Sonia Nieves, M.D., Research Fellow
Mae S. Leonard, Secretary to the Chairperson

DIVISION OF BIOCHEMISTRY

William N. Fishbein, M.D., Ph.D.
Chief
Date of Appointment - September 1965

MISSION

To provide consultation, education, and research in biochemical pathology and toxicology, with particular emphasis on molecular mechanisms.

STAFF

Medical

William N. Fishbein, M.D., Ph.D.

Scientific

John I. Davis, Chemist
John W. Foellmer, Microbiologist

CONSULTATION

Informal consultations were provided in two forms. Summaries were developed and transmitted, as requested, on such items as genetic mutational assays, environmental genotoxicity, principles of freezing and freeze-storage methods, and muscle biochemistry. Case consultations regarding biochemical assays of enzymes, metabolites, and/or genetic mutations were provided when appropriate, principally on frozen muscle biopsy or blood specimens and occasionally on patients requiring specialized provocative tests. The division chief serves as the departmental budget officer and as a member of the AFIP Molecular Biology Committee. He also serves as one of the two certified hyperbaric medical officers on call for chamber dives. He chairs the Process Action Team for Cytogenetics Evaluation at AFIP and has been a member of the Consolidated DOD Genetics/DNA Process Action Team during 1995.

EDUCATION

The division chief contributed lectures to the AFIP staff conferences, as well as extramural invited lectures, and serves as associate editor, Biochemical and Molecular Medicine. The division provides informal training to junior fellows, visiting scientists, student trainees, and staff members undertaking or analyzing experimental research involving molecular biology, spectrophotometry, high-performance liquid chromatography, enzyme stains and assays, electrophoresis, and ultracentrifugation. Dr. Fishbein is also one of two delegates from the subsection Molecular Markers of Disease on the Program Committee of the American Society for Investigative Pathology during 1995 to 1998.

This year involved the following special events:

1. Dr. Fishbein attended the meeting of Experimental Biology and presented a poster discussion on genetic disease.
2. Dr. Fishbein participated in the Walter Reed Intra-City Grand Rounds involving a case of myo-AMP deaminase deficiency.
3. Dr. Fishbein gave a lecture in Dart Auditorium for the staff conference and contributed 2.5 hours of lectures to the Environmental Pathology and Toxicology Course in Washington, D.C., September 18-20, 1995, and 4 hours of lectures to the course in Puerto Rico, May 19-21, 1995.

RESEARCH

This past year, Dr. Fishbein has been developing and teaching some of the modern methods of molecular biology to expand and complement the biochemical and analytical techniques already in use in the division. As these procedures are taught by Dr. Fishbein to his staff, they have been incorporated into the routine program to provide the most up-to-date capabilities for analysis of biological specimens for environmentally generated toxic effects. When taken in conjunction with the direct search for environmental toxins and/or their metabolites, this will provide the department with the widest capabilities for evaluating potential genomic damage and exposure risks. We are now pursuing studies to determine whether there is evidence of increased genomic instability in a series of small population samples with increased exposure to environmental genotoxins due to occupational exposure, to disease and consequent chemotherapy, or to habitat in a contaminated zone. In this regard, Dr. Fishbein prepared a grant application that was submitted to the Gulf War Health Center, which has now been funded for 1996 to 1997 for $110,000. We have also developed a rapid (one-day) allele-specific PCR assay to complement our allele-specific hybridization assay for the founder's mutation in myoadenylate deaminase deficiency. The latter has been applied to the great repository of such cases that we have here at the AFIP. The new assay will simplify the diagnosis of individual cases sent to the AFIP.

PUBLICATIONS

1. Fishbein WN, Foellmer JW, Davis JI. Frequency of the founder mutation causing most cases of myo-AMP deaminase deficiency (mADD). *FASEB J.* 1995;9:A273.
2. Fishbein WN, Davis JI, Foellmer JW. Prevalence of the double C>T transition in exon 2,3 of AMPD1 in myoadenylate deaminase deficiency (mADD) and other populations. *J Invest Med.* 1995;43(suppl 2):293A.
3. Fishbein WN, Davis JI, Foellmer JW. Is myo-AMP deaminase deficiency (mADD) in Westerners due solely to a characteristic double mutation? *FASEB J*. 1995;9:A1268.

In addition, three items are in press.

GOALS

Consultation

To improve the speed of obtaining and reporting requested enzyme assays on muscle biopsy specimens and ischemic forearm exercise tests in problematic patients referred for neuromuscular complaints. To add new molecular genetic assays to the diagnostic armamentarium for use on frozen or fresh biopsy specimens or blood samples in evaluating environmental toxins as well as inherited defects.

Education

To improve the awareness among physicians of the role of metabolic myopathies in compromising athletic and work performance and of the role of muscle in the clinical assessment of environmental toxicology. To introduce the concepts and practice of molecular pathology to residents and visiting fellows.

Research

To reevaluate our current program and complete projects in process, while introducing new projects and procedures for implementation.

DIVISION OF CHEMICAL PATHOLOGY

Frank B. Johnson, M.D.
Chief
Date of Appointment - 26 February 1990

MISSION

To provide consultation, education, and research in the diagnosis and interpretation of disease through the application of physical and chemical procedures to tissues and tissue products, to conduct research, and to provide education in related subjects, particularly as related to environmental toxicology.

STAFF

Medical

Frank B. Johnson, M.D.

Scientific

Hazel Marie Jenkins, Histochemical Technologist

Mehdi Yousefi, D.D.S., M.S., Visiting Scientist

Administrative

Rosalie McQuade, Secretary

CONSULTATION

Cases

Description	*Received*
Military	781
Federal (VA/PHS)	1,780
Civilian	34
Interdepartmental	220

In many cases special chemical and physical procedures were applied, including x-ray diffraction, infrared absorption spectrophotometry, transmission electron microscopy, scanning electron microscopy, energy dispersive x-ray analysis, wet chemical analysis, microscopic histochemistry, and radio frequency plasma reactions. The application of scanning electron microscopy with energy dispersive x-ray analyses is now again possible, since the replacement of the previously damaged instrument on 17 August 1994.

EDUCATION

Dr. Johnson served as a member of the faculty to two histotechnology courses, gave two lectures at the AFIP Professional Staff Conference, and contributed 2.5 hours of lectures to the Environmental Pathology and Toxicology Course in Washington, D.C., September 18-20, 1995, and 4 hours of lectures to the Symposium on Analytical and Molecular Biological Techniques in Environmental Toxicology and Pathology, May 20-21, 1995, in Puerto Rico.

RESEARCH

This past year research activities have concentrated on the development and refinement of methods for identification and characterization of foreign materials in tissues. Studies in the utility of quantitative infrared spectrophotometry and x-ray crystallography are still in progress.

PUBLICATIONS

1. Johnson FB, Oertel YC, Ammann K. Sialoadenitis with crystalloid formation: a report of six cases diagnosed by fine needle aspiration. *Diagn Cytopathol.* 1995;12:76-80.
2. Olsen JH, Schulgen G, Boice JD, Whysner J, Travis LB, Williams GM, Johnson FB, McGee JO'D. Antiepileptic treatment and risk for hepatobiliary cancer and malignant lymphoma. *Cancer Res.* 1995;55:294-297.

GOALS

Consultation

1. Reduce turnaround time for reports.
2. Increase utilization of infrared microscopy for diagnoses.

Education

1. Prepare a set of transparencies illustrating pathogenic particulates in tissue.

Research

1. Continue involvement in a study of the effects of silicone implants.
2. Continue to investigate methods for particulates in tissue.
3. Continue to serve as chairperson, Human Use Committee, WRAIR.

DIVISION OF ENVIRONMENTAL TOXICOLOGY

Victor F. Kalasinsky, Ph.D.
Chief, Division of Environmental Toxicology
Date of Appointment - 25 September 1989

MISSION

To conduct a program of consultation, education, and research in environmental toxicology through the development of techniques for analysis of tissue and the determination of the causes of injury to human and animal tissue.

STAFF

Scientific

Victor F. Kalasinsky, Ph.D., Division Chief
Jose A. Centeno, Ph.D., Research Chemist
(A) Maiella L. Ramos, Ph.D., Research Fellow
(A) Mary Ann Sonoda, Laboratory Technician
(D) Anton M. Gantt, SSGT, USAF, Division NCOIC
(A) Jennifer Sampson, HM3, USN, Division NCOIC
(D) Timothy W. DeWitt, SPC, USA, Biological Laboratory Assistant
(D) Brenda J. Rudyk, SPC, USA, Laboratory Technician

Administrative

(A) Patricia Ashburn, Medical Records Technician
(D) Patricia Ashburn, Medical Records Technician
(A) Kim Knight, Medical Records Technician

CONSULTATION

Cases

Description	*Received*	*Reported*
Surgical	1,519	1,519
Autopsies	3	3
Military/Federal	1,480	1,480
Intramural	49	49
Civilian	42	42

RESEARCH

New instrumentation acquired during the year included a near infrared spectrophotometer. This instrument will be used to monitor various materials in blood.

This year we have been engaged in research described in eight approved protocols:

An Infrared Microspectroscopic Study of Extracellular Matrix Proteins in Keratoconic Corneal Stroma. (Centeno, Kalasinsky, and Specht, formerly of Ophthalmic Pathology)

Characterization of Asbestos Fibers in Tissue by Infrared Microspectroscopy. (Kalasinsky, Centeno, and Johnson)

Analysis and Speciation of Toxic Trace Elements in Body Fluids and Environmental Samples. (Centeno)

Evaluation of Kidney Biopsy Material to Measure the Levels of Lead in the Renal Tissue and to Correlate with the Morphologic Changes. (Sabnis, Nephropathology Division, and Centeno)

Military Working Dogs Deployed to Southwest Asia as Sentinels for Human Environmental Exposure during the Persian Gulf War. (Harris and Martinez, Veterinary Pathology, and Kalasinsky)

Prospective Clinical and Laboratory Evaluation of Patients with Silicone Breast Implants: Determination of Silicon Baseline Levels and Molecular Microanalysis of Pathological Specimens Associated with Fibrous Capsules. (Centeno, Kalasinsky, and Panos, Walter Reed Army Medical Center)

In vivo Analytical and Biological Evaluation of Titanium Microfixation Plates. (Centeno and Jorgenson, Walter Reed Army Medical Center)

Assessment of Baseline Levels for Trace Elements and Toxic Heavy Metals in Placental Tissues: Chemical Marker of Menkes Disease. (Centeno and Kaler, NIH)

In Kuwait-related activities, the division is involved with toxicologic studies of autopsy material from the Dover mortuary. This retrospective study is nearly complete. AFIP is also charged with the long-term storage of blood and serum specimens collected from Gulf War veterans (and their families) who are reporting symptoms that might be related to their service in the Gulf region. This effort is part of the DoD's Comprehensive Clinical Evaluation Program (CCEP). A data base for diagnoses of surgical biopsy specimens is also being maintained for Gulf War veterans reporting to VA or military hospitals.

The division is providing toxicologic and chemical analysis support to the Institute's project involving silicone breast implants. Silicone can be characterized in tissue and in whole implants by using infrared and laser Raman microspectrometers.

Research collaborations continue with Lawrence Berkeley Laboratory, University of Maryland, USDA, NOAA, NIH, USGS, DOE, and Universidad Metropolitana, University of Puerto Rico-Mayaguez, and Ponce School of Medicine in Puerto Rico, and Plastic Surgery Services at Walter Reed Army Hospital.

Dr. Centeno served as advisor for a research fellow and a visiting pathology resident.

Drs. Irey, Kalasinsky, and Peterson (Records and Repository) submitted a proposal entitled "A Morphologic Study of Operation Desert Shield/Storm Veterans" to USAMRAA, August 1995.

Dr. Centeno submitted a proposal entitled "Use of Human Tissues in Toxicologic Pathology: Laser Raman Spectroscopy for Structural Studies of Tissues Affected by Environmental and Hazardous Contaminants" to the American Registry of Pathology, April 1995.

EDUCATION

1. A lecture was presented at a course entitled "Lasers in Surgery," held at the Uniformed Services University for the Health Sciences, Bethesda, Maryland, May 4, 1995. (Centeno)
2. A course entitled "Analytical and Molecular Biological Techniques in Environmental Toxicology and Pathology" was organized in Ponce, Puerto Rico, May 19-21, 1995. (Centeno)
3. An AFIP/ARP course entitled "Analytical and Molecular Biological Techniques in Environmental Toxicology and Pathology" was organized in Washington, D.C., August 18-20, 1995. (Centeno)
4. Lectures were presented in the AFIP/ARP course entitled "Environmental and Molecular Biological Techniques in Environmental Toxicology and Pathology," held August 18-20, 1995. (Centeno and Kalasinsky)
5. A series of lectures was presented in a workshop entitled "Trace Elements in Coal: Environmental and Health Significance of Coal Utilitization," held in Piedras Negras, Mexico, August 28-30, 1995. (Centeno)
6. Two lectures entitled "Metal Analysis in Toxicology" and "Pesticide Analysis in Environmental Toxicology" were presented at the University of Maryland Medical School, Baltimore, December 11, 1995. (Kalasinsky)
7. Three high school students spent 8 weeks in the laboratory during the summer learning analytical methods of toxicology. (Centeno and Kalasinsky)
8. A student from the University of Puerto Rico-Mayaguez spent the summer conducting biophysics research. (Centeno)

OTHER ACTIVITIES

Dr. Centeno was nominated to the editorial board of *Toxicologic Pathology*.

Dr. Centeno served as a reviewer for *Spectrochimica Acta Reviews*.

Dr. Kalasinsky served as a reviewer for *Applied Spectroscopy, Journal of Physical Chemistry*, and *Biospectroscopy*.

Dr. Centeno served as a member of the AFIP Research Review Committee and the AFIP Center for Advanced Pathology Advisory Council.

Dr. Kalasinsky served as a member of the ARP Research Committee.

Dr. Centeno served as an academic program reviewer and consultant to the Metropolitan University, Eastern College, and Turabo University in Puerto Rico.

Dr. Centeno served as a member of the Task Force on Science Curriculum Development and Accreditation, the Task Force on Technology and Network Assessment, and the Presidential Advisory Board for the Ana G. Mendez Univerity System, Puerto Rico.

Dr. Centeno coordinated the signing ceremony of a memoranda of agreement (MOA) to conduct research and education activities among the AFIP, ARP, and the DOE Science Consortium composed of Lawrence Berkeley Laboratory, the Ana G. Mendez University System, and Jackson State University.

Dr. Kalasinsky attended the "Workshop on Infrared Microscopy with Synchrotron Radiation," held at the National Institute of Science and Technology, Gaithersburg, Maryland, May 4, 1995.

Dr. Kalasinsky attended a workshop entitled "Lasers in Surgery," held at the Uniformed Services University for Health Sciences, Bethesda, Maryland, September 22, 1995.

The majority of the renovations to a new laboratory area in the building were completed, and a

move to the new area is anticipated in early 1996.

GOALS

Our goals for the year were (1) to continue to improve the capabilities of the laboratory in order to respond more efficiently to requests (internal and external) for toxicologic analyses, (2) to improve the existing quality assurance program, and (3) to seek funding (intramural and extramural) for environmental research being conducted in the division.

PRESENTATIONS

1. January 13, 1995: Washington, D.C., Division of Forensic Toxicology, AFIP, "Determination of Metals in Biological Specimens," Kalasinsky.
2. February 21, 1995: Philadelphia, Pennsylvania, Society for Applied Spectroscopy, Delaware chapter, "Atomic Absorption Spectrophotometry of Biological Samples from Kuwait," Kalasinsky.
3. March 6, 1995: New Orleans, Louisiana, Forty-sixth Pittsburgh Conference, "Infrared and Raman Microspectroscopy in Biomedical Applications," Kalasinsky.
4. March 21-22, 1995: Mayaguez, Puerto Rico, Conference for Remote Sensing and Environmental Monitoring for the Sustained Development of the Americas, "Toxic Elements in Environmental Toxicology: The Chemistry and Speciation of Arsenic, Selenium, and Chromium in the Environment," Centeno.
5. March 29, 1995: Silver Spring, Maryland, National Oceanic and Atmospheric Administration, "Analytical and Spectroscopic Techniques for the Study of Toxic Trace Metals in Environmental Toxicology," Centeno.
6. August 30, 1995: Thessaloniki, Greece, First International Conference on Environmental Toxicology, "GC/MS Characterization of Inhalants in Blood and Tissue," Kalasinsky
7. October 11, 1995: Morgantown, West Virginia, Department of Chemistry, West Virginia University, "Molecular Microanalysis of Biological Tissues Using Infrared and Laser Raman Microspectroscopy," Centeno.
8. November 8, 1995: College Park, Maryland, Department of Civil Engineering, University of Maryland, "Toxic Elements in Environmental Toxicology: the Chemistry and Speciation of Arsenic, Chromium, and Selenium in the Environment," Centeno.

PUBLICATIONS

Abstracts

1. Kalasinsky VF, Centeno JA, Johnson FB, Luke JL. Infrared and Raman microspectroscopy in biomedical applications. In: Proceedings of the Forty-sixth Pittsburgh Conference; March 6-10, 1995; New Orleans, Louisiana.
2. Ibrahim A, Oldham PB, Wang J, Kalasinsky VF, Schultz TP, Conners TE. Rapid characterization of wood pulp lignin by FT-Raman spectroscopy. In: Proceedings of the Forty-sixth Pittsburgh Conference; March 6-10, 1995; New Orleans, Louisiana.
3. Centeno JA, Johnson FB, Kalasinsky VF, Mullick FG. Microspectroscopic evaluation of foreign inclusions in human pathology: the laser Raman microprobe technique. In: Proceedings of the annual meeting of the United States and Canadian Academy of Pathology; March 1995; Toronto, Canada.
4. Centeno JA. Toxic elements in environmental toxicology: the chemistry and speciation of arsenic, chromium, and selenium in the environment. In: Proceedings of the Conference for Remote Sensing and Environmental Monitoring for the Sustained Development of the Americas; March 21-22, 1995; San Juan, Puerto Rico.

5. Centeno JA, Feliu LA, Diaz E, Hernandez SP, Perry DL, Offiah OO, Scott I. Spectroscopic studies on the interaction of arsenic species with glutathione. In: Proceedings of the 209th national meeting of the American Chemical Society; April 2-6, 1995; Anaheim, Calif.
6. Pestaner JP, Mullick FG, Johnson FB, Centeno JA. Calcium oxalate: molecular analysis with Raman microspectroscopy. *Am J Clin Pathol.* 1995;104:343A.
7. Pestaner JP, Mullick FG, Johnson FB, Centeno JA. Calcium oxalate: molecular analysis with Raman microspectroscopy. In: Proceedings of the American Society of Clinical Pathologists and College of American Pathologists Annual Meeting; August 1995; New Orleans, La.
8. Kalasinsky VF. GC/MS characterization of inhalants in blood and tissue. In: Aspects on Forensic Toxicology; Proceedings of the 33rd International Congress on Forensic Toxicology and 1st International Congress on Environmental Toxicology; August 27-31, 1995; Thessaloniki, Greece.
9. Mayer MH, Jorgenson DS, Ellenbogen RG, Crabtree TG, Centeno JA, Johnson FB, Mullick FG, Manson PN. Atomic absorption analysis of titanium microfixation plates of the craniofacial skeleton. In: Proceedings of the Implantable Materials in Facial Aesthetic and Reconstructive Surgery: Biocompatibility and Clinical Applications; October 6, 1995; Montreal, Canada.

In addition, seven journal articles and one book chapter have been submitted for publication.

DIVISION OF ENVIRONMENTAL PATHOLOGY

Nelson S. Irey, M.D., Chairperson

Florabel G. Mullick, M.D.

STAFF

Nelson S. Irey, M.D.
Florabel G. Mullick, M.D., Staff Pathologist
Sonia Nieves, M.D., Research Fellow

CONSULTATION

Cases

Description	*Received*	*Reported*
Surgical	1,647	1,647
Autopsies	16	16
Military/Federal	1,587	1,587
Intramural	103	103
Civilian	60	60

The Kuwait study (combined morphologic/toxicologic) continues. The prospective character of this project has been increased, with the influx of biopsy and autopsy material being contributed from VA and Armed Forces hospitals throughout the country from veterans who had prior service in Kuwait.

There were about 600,000 members of the Armed Forces of the U.S. assigned to the Persian Gulf area during Desert Shield and Desert Storm. During 1995, this department received about 1,500 cases from these veterans. Over 600 of these cases were analyzed and diagnosed during this report period. This task has been the major activity of Dr. Irey. It is predicted that the future illnesses of this group of veterans will receive Dr. Irey's attention over the next few years.

PRESENTATIONS

1. Mullick FG, codirector, organizer, and lecturer for the Spanish course: *Controversias Y Adelantos en Patologia Quirurgica*, given in San Juan, Puerto Rico, May 31 to June 3, 1995. Lecture title: Drug-Induced Liver Disease.
2. Mullick FG, invited lecturer, *Adverse Drug Reactions*, Georgetown University, March 1995.
3. Mullick FG, invited lecturer, *Tissue Reaction to Drugs*, Uniformed Services University of the Health Sciences, December 1995.
4. Mullick FG, invited lecturer, *Adverse Drug Reactions*, Puerto Rico Medical School, October 1995.
5. Mullick FG, invited lecturer, *Drug-Induced Liver Disease,* Update and Review of Anatomic Pathology Course, AFIP Radiologic Education Center, April 1995.
6. Mullick FG, director, organizer, cochair, and lecturer: Symposium on Environmental Pathology and Toxicology at the World Association of Societies of Pathology's XVIII World Congress of Anatomical Pathology, Auckland, New Zealand, October 1995.
7. Mullick FG, invited lecturer, *The Use of Tissue in Toxicologic Pathology*, Ponce School of Medicine, Ponce, Puerto Rico, May 1995.
8. Mullick FG, invited lecturer, *Analytical and Molecular Biological Techniques in Environmental Toxicology and Pathology*, AFIP Radiologic Education Center, August 1995.
9. Mullick FG, invited lecturer, workshop entitled Analytical Techniques in Environmental Pathology and Toxicology, Chemical Congress, Puerto Rico, September 1995. Lecture title: *Use of Human Tissues in Toxicologic Pathology*. Lecture title: *Adverse Drug Reactions in Environmental Pathology Toxicology.*

COMMITTEE PARTICIPATION (EXTRAMURAL):

1. Secretary, International Academy of Pathology
2. Member, Finance Committee, International Academy of Pathology
3. Member, International Organizing Committee, XXI International Congress of the International Academy of Pathology, Budapest, Hungary
4. Cochair, Organizing Committee, and member, Nominating Committee for the History of Pathology Society
5. Member, editorial board of Toxicologic Pathology and section editor of Environmental Toxicologic Pathology section
6. Member, Toxicology's Subcommittee on Permissible Exposure Levels (PEL's) for Military Jet Fuels, National Research Council, National Academy of Science
7. Special consultant for pathology, University of Puerto Rico Medical School

8. Member, editorial board of *Modern Pathology*
9. Member, *Electronic Journal of Pathology and Histology*
10. Member, U.S. Presidential Advisory Board for the Ana G. Mendez University System (AGMUS)
11. Academic program reviewer and consultant, Metropolitan University, Eastern College, and Turabo University in Puerto Rico.
12. Member, Task Force on Technology and Network Assessment for the AGM University System
13. Member, Task Force on Science Curriculum Development and Accreditation for AGMUS

COMMITTEE PARTICIPATION (INTRAMURAL):

1. Member, Executive Committee of the AFIP
2. Chair, Executive Committee of the Medical Staff
3. Chair, Search Committee, CAP, AFIP
4. Chair, Pathology Information Management System Committee, AFIP
5. Member, Resources Management Committee
6. Member, Space Utilization and Management Committee
7. Member, Awards Committee (Military)

PUBLICATIONS

Journal Articles

1. Centeno JA, Luke JL, Kalasinsky VF, Johnson FB, Mullick FG, Panos R. Laser-Raman microprobe identification of pathological inclusions in fibrous capsules associated with breast implants. *Plastic and Reconstructive Surgery*; 1995.

Abstracts

1. Pestaner JP, Mullick FG, Johnson FB, Centeno JA. Calcium oxalate: molecular analysis with Raman microspectroscopy. ASCP and CAP Annual Meeting. *Am J Clin Pathol.* 1995;104:343.
2. Pestaner JP, Mullick FG, Virmani R. Comparison of toxic cardiomyopathy and dilated cardiomyopathy by light microscopy. USCAP, 84th Annual Meeting, Toronto, Canada. *Mod Pathol.* 1995;8:29A.
3. Centeno JA, Johnson FB, Kalasinsky VF, Mullick FG. Microspectroscopic evaluation of foreign inclusions in human pathology: the laser Raman microprobe technique. USCAP, 84th Annual Meeting, Toronto, Canada. *Mod Pathol*. 1995;9:194A.

In addition, one article has been accepted for publication.

DIVISION OF MUTAGEN PATHOLOGY

David B. Busch, M.D., Ph.D.
Chief

STAFF

David B. Busch, M.D., Ph.D., Staff Pathologist
Roberta Bliss Albert, Laboratory Technician
(A) Deborah A. White, Laboratory Technician

CONSULTATION

Cases

Description	*Received*	*Reported*
Surgical	22	22
Autopsies	1	1
Military/Federal	1	1
Intramural	0	0
Civilian	22	22

Workload

Dr. David Busch is working approximately 50 to 60 hrs/week on the average (worst week approximately 70 hrs).

Ms. White was recruited by ARP in mid-1995 as a ≥ 19 hour/week employee. She is a law student at American University with an interest in patent law dealing with biotechnology and has a tissue culture background. She is expected to remain with the lab until early 1998. She has been oriented to DNA microinjection work. Ms. White will be working mostly on basic research identifying the phenotype of mutant CHO cells with minimal UV sensitivity for the period October 1995 to September 1996. She has also learned the diagnostic autoradiography assays for xeroderma pigmentosum (XP) and Cockayne's syndrome (CS), which will occupy much of her time after she finishes the basic research work. She assists with the lab's diagnostic work (xeroderma pigmentosum and Cockayne's syndrome autoradiography assays; UV survival curves of human fibroblast cultures).

Ms. Albert discontinued her work as a laboratory technician in 1995 and now works approximately 3 hrs/week on this lab's CD-ROM multimedia production project (see "EDUCATION").

Consultation cases

1. Signed out 11 unscheduled DNA synthesis assay cases to rule out xeroderma pigmentosum (approximately 30 hours/case), with the first of two assays required for sign out performed on five additional cases.

2. Accessioned the first 10 suspected cases of Cockayne's syndrome, with the first of two RNA assays completed and the second assay awaiting final data analysis for five of these cases (approximately 30 hours work/sign out of RNA assay case). This represents the introduction of a new diagnostic autoradiography test to the laboratory, which is not available elsewhere in the country except for research purposes. The availability of the test has been publicized by

the newsletter of Share and Care, the Cockayne's syndrome organization, so that it is becoming known that US CS patients can again be diagnosed by a US laboratory.

3. Performed approximately 100 UV survival curve studies on human fibroblast cultures (approximately 3 hours work per assay) including controls and accessioned consultation cases. This represents the introduction of an additional diagnostic test to the laboratory, which is not available elsewhere in the country except for research purposes. The test allows identification of xeroderma pigmentosum variant patients and permits prescreening of suspected xeroderma pigmentosum and Cockayne's syndrome patients in order to determine if they merit the more labor-intensive, more expensive autoradiography studies and as an independent method for quantifying the severity of their deficiency.
4. Performed the first two known cases of depleted uranium injury using autoradiography, using materials from injured Gulf War veterans.
5. Continue to get extremely rare radiation consult cases from other AFIP departments and to not be designated recipient of newly accessioned AFIP radiation injury cases.
6. Selection of vendor for Major Medcase purchase of x-ray machine intended for laboratory diagnosis of patients with ataxia telangiectasia (congenital x-ray sensitivity with high risk of cancer).
7. Received approximately $15,000 in gross receipts from XP, CS, and UV survival studies during 1995, mostly from case contributors. About half of the cases were not reimbursed due to (a) the poverty of family, with no other available source of funding for testing; (b) the refusal of the state health program to pay for out-of-state laboratory testing; (c) the refusal of the insurance company to pay for unusual lab tests; or (d) it being a military case. Even with the current charges of $950 for XP and CS assays and $500 for UV survival study, it is difficult to pay for the technician's salary. (Note: Dr. Busch is doing the technician's half of the work during the period of the ARP research grant described below, leaving much less time for other work.)
8. Unsuccessfully applied to the National Organization of Rare Disorders for a grant to fund complementation testing of XP and CS patients.

EDUCATION

1. No VA/HQAP program assignments during 1995.
2. Initial organizational work for another 3-day AFIP/ARP short course on radiation and chemotherapy injury, scheduled for September 7-9, 1996, at Tysons Corner, Va., will include a new 5-hour session on congenital sensitivity to DNA-damaging agents, emphasizing xeroderma pigmentosum, Cockayne's syndrome, and ataxia telangiectasia. The unusual features of this course will be (1) two half-hour grand rounds and (2) round-table panel discussions on the impact of CLIA88 on laboratory diagnosis of rare genetic diseases and on reimbursement of laboratories for testing for rare genetic diseases. Confirmed panelists include DNA repair researchers James Cleaver, Jan Hoeijmakers, and Ken Kraemer; Teresa Wall; Caren Mahar; and Jess Thoene (chairman of the board of directors of the National Organization for Rare Disorders and chair of the National Commission on Orphan Diseases, 1987-1989). It is likely, but not confirmed, that the panel will also have representatives from the College of American Pathologists, the Health Care Financing Administration, and the office of US Congressman Bill Archer (Texas), who introduced a bill to amend CLIA88. Efforts also are underway to obtain a panelist from the office of US Congressman John Dingell, who introduced CLIA88 to Congress, and to recruit a representative of *The News Hour*, with Jim Lehrer as panel chair.

   Journals that will run ads for the course include: *International Journal of Radiation Oncology, Biology, Physics; Journal of Clinical Oncology; Journal of Rare Diseases; Archives of Pathology and Laboratory Medicine; American Journal of Human Genetics*; and *Archives of Dermatology.* Some of these ads will also mention ARP study sets on radiation injury, substance abuse,

and chemotherapy and chemical warfare injury, which will bring additional funds to the Radiation Pathology Registry, and the lab's consult program for reviewing suspected cases of XP, CS, and XP variants, which should lead to an increase in submission of consults to the lab.

A course brochure is being prepared, which again mentions the study sets and the lab consult program. Approximately 20,000 brochures will be mailed out to members of the American Society of Clinical Oncology, the American Society of Therapeutic Radiology and Oncology, the US and Canadian Academy of Pathology, and the Association of Residents in Radiation Oncology, among others.

3. Excellent progress is being made on a CD-ROM multimedia production project to prepare a 30-minute documentary on Cockayne's syndrome and xeroderma pigmentosum and their laboratory diagnosis. Accomplishments include: (a) videotaping of a 3-minute minilecture on XP by XP researcher James Cleaver (a similar minilecture on CS by Dutch DNA repair researcher Jan Hoeijmakers was obtained in late 1994); (b) visits to the homes of two patients (one with XP and one with CS); (c) videotaping of a slide-staining demonstration by AFIP histotechician Julie Wilson; (d) production of software to allow the selection of different features of the CD-ROM from different menus; and (e) incorporation of some of the videotaped materials into PC audiovisual (*.AVI) files. Note: Mr. Jay Keating is scheduled to give a 30-minute presentation on this project and on CD-ROM multimedia and its production in general at a future AFIP staff conference.
4. Upgraded the lab Pentium PC to include a 600 dpi color scanner with optical character recognition software.
5. Hosted the videotaping of the lab by a French independent film production crew (XL Productions) for their feature on XP. The feature includes footage of ARP technician Deborah White demonstrating steps in the assay, an interview with David Busch, and a demonstration of case sign out at NIH with XP researcher Ken Kraemer and David Busch. This feature will be one of a series of hour-long documentaries on "Children of Courage," covering different rare genetic diseases, which is expected to be shown on French TV early in 1996.
6. Revised and updated the ARP 35-mm slide study set on radiation pathology.
7. The slide study set net income to the Radiation Pathology Registry for 1995 is approximately $3,000.
8. Lectured on radiation injury, chemotherapy injury, tissue culture equipment, and tissue culture methodology at Dr. Centeno's AFIP/ARP short courses in Puerto Rico and at the AFIP Callender Laboratory.

RESEARCH

1. Completed 14 additional unscheduled DNA synthesis autoradiography studies for research purposes.
2. CHO (FAECB) UV mutant project

   (a). Submission to *Mutation Research* of a manuscript entitled "A FAECB CHO Mutant, UV40, That Is Sensitive to Diverse Mutagens and Represents a New Complementation Group of Mitomycin C Sensitivity" by David B. Busch, et al., describing the identification of a new rodent UV mutant (equivalent to the discovery of a new DNA repair gene) that is suspected to be a homolog of one of the forms of human congenital pancytopenia (Fanconi's anemia (FA)), which predisposes to hematologic malignancies. Collaborator Larry Thompson at Livermore incidentally reports apparent success in using the mutant to clone the homologous human DNA repair gene, which if a FA gene would mean the cloning of a human antioncogene.

   (b). Performance by laboratory technician Deborah White of UV survival curve studies with

and without caffeine on several slightly UV-sensitive CHO mutants. Two mutants that were derived from xeroderma pigmentosum-like parental line are showing sensitization to UV by caffeine, and thus may be regarded as being concurrently XP-like and XP variant-like, i.e., as simultaneous laboratory models for two different human genetic diseases causing UV sensitivity.

3. The silicone microinjection project was dropped due to lack of ARP support; technician Roberta Bliss Albert reported success in performing cytoplasmic microinjection of low-viscosity silicone into cytoplasm of cultured human fibroblasts before the project was terminated.
4. No research meetings attended due to budgetary constraints.
5. A $16,000 intramural (ARP) grant was approved for funding the CHO project from October 1995 to September 1996.

BREAST IMPLANT REGISTRY

James L. Luke, M.D.

CONSULTATION

Cases

Description	*Received*	*Reported*
Surgical	103	103
Autopsies	0	0
Military/Federal	0	0
Intramural	5	5
Civilian	103	103

Case consultations from pathologists regarding the presence of silicone in breast implant capsules. (LUKE, KALASINSKY)

Analysis of the forensic pathology aspects of cases submitted to the Investigative Support Unit, Critical Incident Response Group, FBI Academy, Quantico, Virginia. (LUKE)

Discussions are in progress to develop a more coordinated operational relationship between the AFIP and various elements of the FBI Laboratory and the FBI Critical Incident Response Group. (LUKE)

RESEARCH

The project initiated in mid-1993 to study the pathologic and certain biophysical aspects of

silicone breast implants continues. Fifteen military departments of pathology have been invited to participate in this prospective study. Examinations include light microscopy and scanning electron microscopy/energy dispersive x-ray analysis, Fourier transform infrared and laser Raman spectroscopy, and atomic absorption spectrophotometry. Through 1995, 121 cases have been accessioned into this project. (LUKE, KALASINSKY, CENTENO, JOHNSON)

A collaborative project correlating clinical changes in breast implant patients with morphological and chemical findings has been initiated with the Plastic Surgery and Rheumatology Departments at Walter Reed Army Medical Center. (KALASINSKY, CENTENO, LUKE)

EDUCATION

1. Presentation of interim findings of the silicone breast implant project to the AFIP Scientific Advisory Board and to the Board of the American Registry of Pathology. (LUKE)
2. Forensic Pathology. Lecture to second-year medical students at the General Pathology Course, Georgetown University School of Medicine. (LUKE)
3. Forensic Pathology Seminar. A series of lectures for residents in the Department of Pathology, Georgetown University Medical Center. (LUKE)
4. Death by Asphyxia. Lecture at AFIP course in Basic Forensic Pathology. (LUKE)

PUBLICATIONS

One article is in preparation.